Paper No. 49

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

Ex parte GARY R. GROTENDORST, and
NAOKO IIDA

Appeal No. 2002-0427
Application No. 08/179,656

ON BRIEF

Before MILLS, GRIMES, and GREEN, Administrative Patent Judges.

GREEN, Administrative Patent Judge.

DECISION ON APPEAL

This is a decision on appeal under 35 U.S.C. § 134 from the examiner's final rejection of claims 1, 3, 5, and 23-26. Claim 6 is also pending and the examiner has indicated that it is allowable. See Paper No. 33, mailed July 13, 1999. Claim 1 is representative of the claims on appeal and reads as follows:

1. A purified protein consisting of Leukocyte Derived Growth Factor 2 (LDGF2) having immunoreactivity and an amino acid sequence which differs from the sequence shown in SEQ ID NO: 17 by an amino acid(s) substitution, deletion, or insertion which does not affect the reactivity of the protein.

The examiner relies on the following references:

Tischer et al. (Tischer), "Vascular endothelial growth factor: A new member of the platelet-derived growth factor gene family," Biochemical and Biophysical Research Communication, Vol. 165, No. 3, pp. 1198-1206 (1989)

Bowie et al. (Bowie), "Deciphering the Message in Protein Sequences: Tolerance to Amino Acid Substitutions," Science, Vol. 247, pp. 1306-1310 (1990)

Wells, "Additivity of Mutational Effects in Proteins," Biochemistry, Vol. 29, No. 37 pp. 8509-8517 (1990)

Robinson, "Growth factors in wound healing," TibTech, Vol. 10, pp. 2-3 (1992)

Meyer-Ingold, "Wound therapy: growth factors as agents to promote healing" TibTech, Vol. 11, pp. 387-392 (1993)

Pilbeam et al. (Pilbeam), "Comparison of the Effects of Various Lengths of Synthetic Human Parathyroid Hormone-Related Peptide (hPTHrP) of Malignancy on Bone Resorption and Formation in Organ Culture," Bone, Vol. 14, pp. 717-720 (1993)

Daniel et al. (Daniel), "Mapping of Linear Antigenic Sites on the S Glycoprotein of a Neurotropic Murine Coronavirus with Synthetic Peptides: A Combination of Nine Prediction Algorithms Fails to Identify Relevant Epitopes and Peptide Immunogencity Is Drastically Influenced by the Nature of the Protein Carrier," Virology, Vol. 202, pp. 540-549 (1994)

Callard et al. (Callard), The Cytokine FactsBook, p. 31 (1994)

Ngo et al. (Ngo), Computational Complexity, Protein Structure Prediction, and the Levinthal Paradox," The Protein Folding Problem and Tertiary Sturcture Prediction, pp. 491-495 (1994)

Claims 1, 3, 5, and 23-26 stand rejected under 35 U.S.C. § 112, first paragraph, as nonenabled.

Claims 1, 3, 5, and 23-26 stand rejected under 35 U.S.C. § 112, first paragraph, as lacking an adequate written description in the specification.

We affirm the written description rejection and do not reach the enablement rejection.

Background

The specification discloses that platelet-derived growth factors (PDGF) "has some limitations regarding its usefulness in wound repair. First, PDGF is a dimeric glycosylated protein which is difficult and expensive to produce. Second, PDGF is a relatively large molecule which also makes it more difficult to produce recombinantly or chemically than smaller molecules." Page 2.

The specification discloses a protein, Leukocyte Derived Growth Factor 2 (LDGF2), "having PDGF-like activity. LDGF2 reacts with PDGF receptors and possesses mitogenic and/or chemotactic activity for various cell types, particularly connective tissue cells. LDGF2 may be used as the active ingredient in therapeutic compositions, e.g. wound healing compositions." Page 2. The specification also discloses that LDGF2 is structurally similar to another protein, known as LDGF1, "in that the first 49 amino acids of each protein are the same. The last 12 amino acids of LDGF2 differ significantly from the corresponding portion of LDGF1." Id.

The specification also states that

> [t]he term "LDGF" is intended to include LDGF2, functional equivalents thereof, and antigenic fragments thereof. The term functional equivalents is intended to include proteins which differs [sic] in amino acid sequence from the LDGF2 amino acid sequence (SEQ ID NO:17) . . . but wherein the differences are of a nature which allows the modified protein to behave in the same or similar manner as LDGF2. For example, the modification may be to an amino acid which is not directly involved in LDGF2's ability to perform its intended function of reacting with the PDGF receptor. For example, the modification may be an amino acid(s) substitution, deletion or insertion.

Page 5. The specification goes on to say that the first 49 amino acids of LDGF2 appears to be involved in PDGF receptor-binding, and that modifications outside of that area (i.e., in the C-terminal 12 amino acids) "may not [a]ffect LDGF2's ability to react with the PDGF receptor and/or ability to behave as a mitogen or chemoattractant." Id.

Discussion

Claim 1 is directed to a protein "consisting of Leukocyte Derived Growth Factor 2 (LDGF2)," "having immunoreactivity," and having "an amino acid sequence which differs from the sequence shown in SEQ ID NO:17 by an amino acid(s) substitution, deletion or insertion which does not affect the reactivity of the protein." Since Appellants have presented no arguments to show the separate patentability of the claims, claims 3, 5, and 23-26 stand or fall with claim 1. See 37 CFR § 1.192(c)(7); In re Kaslow, 707 F.2d 1366, 1376, 217 USPQ 1089, 1096 (Fed. Cir. 1983) ("Since the claims are not separately argued, they all stand or fall together.")

The examiner rejected the claims under 35 U.S.C. § 112, first paragraph, as lacking an adequate written description in the specification. The examiner found that

> [t]he claims recite a structurally undefined LDGF2 and non-naturally occurring analogues of a structurally undefined LDGF2. The specification discloses one amino acid sequence for LDGF2 (SEQ ID NO:17) and states that the term "LDGF2" [sic, "LDGF"] embraces structures that differ from SEQ ID NO:17 but are functional equivalents.

Examiner's Answer, page 10. She concluded that "the specification lacks an adequate written description for variants and non-naturally occurring analogues of the LDGF2 of SEQ ID NO:17" because, among other reasons, "[w]ith the exception of [SEQ ID NO:17], the skilled artisan cannot envision the detailed chemical structure of the encompassed proteins, and therefore conception is not achieved until reduction to practice has occurred," and "[o]ne cannot describe what one has not conceived." Id., page 11, citing Fiers v. Revel, 984 F.2d 1164, 25 USPQ2d 1601 (Fed. Cir. 1993), and Fiddes v. Baird, 30 USPQ2d 1481 (Bd. Pat. App. Int. 1993).

The Federal Circuit has recently addressed the written description requirement in the context of DNA-related inventions. See Enzo Biochem, Inc. v. Gen-Probe Inc., 296 F.3d 1316, 63 USPQ2d 1609 (Fed. Cir. 2002). The Enzo court adopted the standard that "the written description requirement can be met by 'showing that an invention is complete by disclosure of sufficiently detailed, relevant identifying characteristics . . . i.e., complete or partial structure, other physical and/or chemical properties, functional characteristics when coupled with a known or disclosed correlation between function and structure, or some combination of such characteristics.'" Id. at 1324, 63 USPQ2d at 1613 (emphasis omitted, bracketed material in original).

While the invention at issue in Enzo was DNA, the holding of that case would also seem to apply to a claimed protein. The court adopted its standard from the USPTO's Written Description Examination Guidelines. See 296 F.3d at 1324, 63 USPQ2d at 1613 (citing the Guidelines). The Guidelines apply to

proteins as well as DNAs. See id. (citing Guidelines' example of an antibody defined by its binding affinity). See also id. at 1328-29, 63 USPQ2d at 1616 ("Even if a claim is supported by the specification, the language of the specification, to the extent possible, must describe the claimed invention so that one skilled in the art can recognize what is claimed. . . . The disclosure must allow one skilled in the art to visualize or recognize the identity of the subject matter purportedly described.").

In this case, we agree with the examiner that the claimed genus of proteins is not adequately described in the specification. Claim 1 is directed to a protein that "consist[s] of Leukocyte Derived Growth Factor 2 (LDGF2)," "ha[s] immunoreactivity," and differs from SEQ ID NO:17 by at least one substitution, deletion, or insertion "which does not affect the reactivity of the protein." The specification, however, does not describe in detail any specific protein falling within the claimed genus. The only specific protein described in the specification is LDGF2, which has the sequence of SEQ ID NO:17. This protein, however, is specifically excluded from the scope of claim 1. The specification does not describe a single protein that differs from SEQ ID NO:17 by even a single amino acid, in such a way that it "does not affect the reactivity of the protein."

The specification does not describe the genus of claimed proteins in general terms. It does not describe where in the protein the deletions, substitutions, or insertions could be made without "affect[ing] the reactivity of the protein," nor does it describe the types of variation that would affect reactivity, or how much the claimed proteins could vary from in sequence from SEQ ID NO:17

before the variation would "affect the reactivity of the protein." The specification does not even describe how much effect on the protein's "reactivity" is considered to be "affect[ing] the reactivity."

Thus, the specification does not describe the claimed genus of proteins in terms that would allow those skilled in the art to recognize that the inventors invented what is claimed. See In re Wertheim, 541 F.2d 257, 262, 191 USPQ 90, 96 (CCPA 1976). ("It is not necessary that the application describe the claim limitations exactly, . . . but only so clearly that persons of ordinary skill in the art will recognize from the disclosure that appellants invented processes including those limitations.").

In terms of the Enzo test, the instant specification does not provide the complete structure of any of the claimed proteins, since the only complete structure recited in the specification is that of SEQ ID NO:17, the only sequence specifically excluded from the instant claims. Nor does the specification provide any partial structures for any of the claimed proteins, except for some (uncharacterized) proteins that might differ from SEQ ID NO:17 only by addition of one or more amino acids at either end. None of the other proteins defined by the claims—those that differ from SEQ ID NO:17 by one or more additions, substitutions, or deletions—would have the structure of SEQ ID NO:17 as their complete or partial structure. Nor does the specification provide physical or chemical properties of the claimed proteins that would adequately define them to those skilled in the art. Finally, the specification describes functional properties of the claimed proteins (specifically, that they "ha[ve] immunoreactivity" and differ

from SEQ ID NO:17 in a way that "does not affect the reactivity of the protein"), but those functional properties are not correlated with any particular structural features. Thus, the instant specification does not adequately describe the claimed genus of proteins.

Appellants argue that they have adequately described the claimed genus by describing structural features which are common to the members of the genus. See the Appeal Brief, page 9:

> [T]he claimed features taught by Appellants which are common to the members of the claimed genus include an LDGF2 protein which include (1) having an amino acid sequence which differs from the sequence shown in SEQ ID NO:17 by an amino acid(s) substitution, deletion or insertion in a region selected such that it does not affect the reactivity of the protein, and (2) having immunoreactivity.

Appellants go on to argue that they also provide methods of making "functional equivalents" and "antigenic fragments" of LDGF2 and conclude that "the claimed genus is defined by structural and functional features that are adequately described in the specification, recited in the claims, and commonly possessed by its members. These features are common to a substantial portion of the claimed genus." Id., pages 9-10.

Finally, Appellants argue that the instant specification

> present[s] SEQ ID NO:17 as a representative of the claimed genus. This member of the genus exemplifies all of the structural and functional features included in the claims and taught in the specification which are common among a substantial portion of the members of the claimed genus. Appellants further submit that disclosure of this member of the claimed genus constitutes a "representative number" of species.

Id., page 10.

These arguments are not persuasive. To take Appellants' last argument first, SEQ ID NO:17 cannot be "representative of the claimed genus" nor can it constitute a "representative number" of species of the genus. SEQ ID NO:17 is expressly not a part of the claimed genus. The members of the claimed genus are required to differ in sequence from SEQ ID NO:17; thus, SEQ ID NO:17 is the only sequence that cannot be within the claimed genus. A species cannot be representative of a genus of which it is not a part.

Second, we do not agree that the specification's general discussion of either products of methods provides a description that is adequate to meet the requirements of 35 U.S.C. § 112, second paragraph. Appellants have pointed to no specific, structural features that would have been recognized by those of skill in the art as common to LDGF2 variants "having immunoreactivity" or retaining the "reactivity" of LDGF2. The specification simply provides no structural answers to the pertinent questions: what types of amino acid changes can be made, how many, and in what part(s) of the molecule, without eliminating the "immunoreactivity" or changing the "reactivity" of LDGF2? Thus, the specification does not provide a structural description of how the claimed LDGF2 variants differ from SEQ ID NO:17, and therefore fails to adequately describe the claimed genus.

The examiner also rejected the claims for failing to meet the enablement requirement of 35 U.S.C. § 112, first paragraph. Since we have already concluded that the claims are unpatentable under that section of the statute because they lack an adequate written description, we need not consider

whether they are also nonenabled. Therefore, we do not reach the examiner's enablement rejection.

Other Issues

If the claims are re-filed or subject to further prosecution, the examiner should consider whether the present language of the claims is sufficiently definite to pass muster under 35 U.S.C. § 112, second paragraph; that is, whether "the claims, read in light of the specification, reasonably apprise those skilled in the art and are as precise as the subject matter permits." Hybritech, Inc. v. Monoclonal Antibodies, Inc., 802 F.2d 1367, 1385, 231 USPQ 81, 94-95 (Fed. Cir. 1987).

The claims contain several phrases that give rise to ambiguity. First, claim 1 is directed to a protein that "consist[s] of Leukocyte Derived Growth Factor 2 (LDGF2)." The specification discloses that LDGF2 has the amino acid sequence of SEQ ID NO:17. The first part of the claim therefore would seem to suggest the claimed protein has the amino acid sequence of SEQ ID NO:17. The claim goes on to state, however, that the claimed protein differs from SEQ ID NO:17 by at least one substitution, deletion, or insertion. These limitations appear to conflict: how can a protein consist of LDGF2 if it can be anything but SEQ ID NO:17?

In addition, claim 1 states that the claimed protein has "immunoreactivity." The specification does not provide an express definition of "immunoreactivity," suggesting that the term is being used in its art-recognized meaning; specifically, the protein is reactive with components of the immune system (e.g., antibodies). The prosecution history, however, suggests a different meaning: when the

present claim language was first introduced, Appellants described an enclosed declaration as showing that "the amino terminal portion of LDGF is responsible for the PDGF-like biological activity of the molecule, i.e., immunoreactivity." While an applicant can be his own lexicographer, any alternative meaning must be clearly indicated in the specification. See Optical Disc Corp. v. Del Mar Avionics, 208 F.3d 1324, 1334, 54 USPQ2d 1289, 1295 (Fed. Cir. 2000) ("Without evidence in the patent specification of an express intent to impart a novel meaning to a claim term, the term takes on its ordinary meaning.").

Finally, the claims state that the amino acid change in the claimed protein vis-à-vis SEQ ID NO:17 "does not affect the reactivity of the protein." The particular "reactivity" that remains unaffected is another source of ambiguity. The specification mentions LDGF2 functions of "reacting with the PDGF receptor" (page 5, line 7), as well as "reacting with the PDGF receptor and/or acting as a mitogen or chemoattractant." LDGF2 may have other reactivities that are unknown.

"[D]uring patent prosecution when claims can be amended, ambiguities should be recognized, scope and breadth of language explored, and clarification imposed." In re Zletz, 893 F.2d 319, 322, 13 USPQ2d 1320, 1322 (Fed. Cir. 1989). If the instant claims are subject to further examination, the examiner should consider whether the language of the claims is sufficiently definite.

Summary

We affirm the examiner's rejection for lack of written description, do not reach the rejection for nonenablement, and recommend that the definiteness of the claims be considered in any further prosecution.

No time period for taking any subsequent action in connection with this appeal may be extended under 37 CFR § 1.136(a).

AFFIRMED

Demetra J. Mills Administrative Patent Judge	)
Eric Grimes Administrative Patent Judge	) BOARD OF PATENT) APPEALS AND) INTERFERENCES
Lora M. Green Administrative Patent Judge	)

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